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Statins for multiple sclerosis

Timothy Vollmer and colleagues (May 15, p 1007)[1] provide evidence that treatment with 80 mg of simvastatin inhibits the inflammatory components of multiple sclerosis. Their study is not, however, "the first to provide some evidence of an effect with a statin in multiple sclerosis", as stated by Chris Polman and Joep Killestein in their Commentary.[2]

In 2003, we reported[3] the results of an observational study of seven female patients who had relapsing-remitting disease after 1 year of monotherapy with 40 mg of lovastatin. In agreement with Vollmer and colleagues' findings, we noted a reduction in the mean number of gadolinium (Gd)-enhancing lesions and no great differences between pretreatment and treatment expanded disability status scores. Three patients remained free of relapses, and the mean annual relapse rate decreased during the year. However, we did detect new lesions on T2-weighted images in five patients at the end of the study. Six people have now completed 2 years of lovastatin monotherapy; three patients had relapses and developed new T2-weighted lesions during the second year of treatment.

Our results suggest that the reduction in Gd-enhancing lesions observed by Vollmer and colleagues after 6 months of treatment cannot ensure an inhibitory effect on the progression of the disease, which is only testable with longer periods of follow up.

As Polman and Killestein note,[2] the differential anti-inflammatory potency of statins should be considered in this context, since they can also be dose-dependent. However, experimental evidence[4] suggests that high doses of statins, which pass the blood-brain barrier, could interfere with neural repair mechanisms. Hence, we feel that the widespread use of these drugs in patients with multiple sclerosis cannot be recommended until randomised controlled trials have been done to address these issues.

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Timothy Vollmer and colleagues[1] report the effective use of a drug that is generally considered safe in the treatment of relapsing-remitting multiple sclerosis, which is very promising. Although no serious adverse drug effects arose during the study, three patients complained of muscle weakness, one had an increased creatinine phosphokinase concentration, and two had abnormal liver-function test results. This high proportion of adverse effects could be a direct consequence of the fairly high daily dose of simvastatin used. We caution against the chronic administration of such a high dose.

In 2000 and 2001 (before the cerivastatin withdrawal episode), our Regional Centre of Pharmacovigilance recorded 13 cases of raised creatinine phosphokinase concentrations in individuals prescribed simvastatin (n=2), atorvastatin (n=6), cerivastatin (n=2), fluvastatin (n=1), or pravastatin (n=2). In all cases, doses complied with the marketing authorisations, but the highest creatinine phosphokinase values arose in those patients given the highest doses. Median treatment duration was equivalent to that reported by Vollmer and colleagues. The French National Pharmacovigilance Data Base includes more than 20 cases of rhabdomyolysis, occurring during simvastatin use at recommended dose.

Although simvastatin, lovastatin, and mevastatin inhibit proliferation of peripheral blood mononuclear cells in a dose-dependent manner they should be regarded as potentially myotoxic, and high doses should be used cautiously in the long term.[2] We acknowledge the treatment breakthrough, but think muscle enzyme values should be closely monitored so as to avoid any inappropriate and unwanted interruption of treatment. As statins begin to be available without prescription in some countries, this issue is likely to become a greater concern.

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Authors' reply

We appreciate the comments of Armando Sena, Rui Pedrosa, and Graça Morais. Our study was an exploratory study and is suggestive of benefit from oral simavastatin therapy in patients with relapsing forms of multiple sclerosis by an MRI surrogate measure. Their data seem similar to ours. We agree that neither of these studies provides adequate support for the use of statins as a treatment for multiple sclerosis outside of well-designed clinical trials. We also agree that